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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
ANGELL, JON E

ART UNIT	PAPER NUMBER
1635	18

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,442	AUDONNET ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *2,4,6-15 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,16-19 and 21-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Action is in response to the communication filed on 6/11/03, as Paper No. 17. the amendment has been entered. Claims 1, 4, 5, 18 and 19 have been amended. Claims 1-38 are currently pending in the application and are addressed herein.

2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Election/Restrictions

3. Claims 2, 3, 6-15 and 20 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim, for the reasons of record. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

4. This application contains claims 2, 3, 6-15 and 20 drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1, 4, 5, 16-19 and 21-38 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 210 and 211 of copending Application No. 09/760,574. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to method of inducing an immunological response against BRSV in a bovine comprising administering to the bovine the same compositions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

3. Applicant's arguments filed 6/11/03 have been fully considered but they are not persuasive.

Applicants argue that claims 210 and 211 of '574 are drawn to a method of inducing an immune response against a bovine pathogen (claim 210), specifically BRSV (claim 211). Applicants argue that the claims of '574 do not encompass, nor do they render obvious the administration of the composition of claim 1(a) in combination with claim 1(b).

4. In response, the methods of the '574 application and the instant claims are not identical they are not patentably distinct from each other because they are both drawn to method of

inducing an immunological response against BRSV in a bovine comprising administering to the bovine the same compositions.

5. Applicants indicated that, upon allowance , if necessary, a terminal disclaimer would be filed.

Claim Rejections - 35 USC § 112

6. The rejection of claims under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn in view of the claim amendments.

Claim Rejections - 35 USC § 103

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1, 4, 5, 16-19 and 21-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al. (Journ. General Virology 1997, 78:3195-3206) in view of Harris et al. (US Patent 5,719,131; 1998) and further in view of Bonnem et al. (WO 94/01133, listed in IDS as reference AJ) and Baker et al. (US Patent 5,106,733; 1992), for the reasons of record, summarized below.

Taylor teaches a DNA vaccine against a bovine pathogen (specifically, BRSV) comprising a nucleic acid encoding an immunogen of a pathogen of the animal species

considered (here, the F and G proteins of BRSV), under conditions allowing the in vivo expression of this sequence (see p. 3195, abstract; p. 3199, Figure 2; and p. 3200, under "Effect of vaccination on BRSV infection").

Taylor does not teach that: 2) the vaccine comprises a cationic lipid containing a quaternary ammonium salt (such as DMRIE and DOPE); 2) the vaccine comprises a GM-CSF protein of the animal species considered or a plasmid encoding said GM-CSF protein.

Harris teaches a cationic amphiphile comprised of DMRIE and DOPE, which can be complexed to therapeutic molecules and used to facilitate the transport of the therapeutic molecules (such as plasmid DNA) into target cells in a subject (see abstract; and column 40, lines 45-52). Harris teaches "the complex structure, behavior and environment presented by an intact tissue that is targeted for intracellular delivery of biologically active molecules often interfere substantially with such delivery..." Administration of the amphiphile facilitates the transport of the therapeutic molecules into cells.

Bonnem teaches that GM-CSF can be used as a vaccine adjuvant for enhancing the immune response of a mammal to a vaccine comprising administering to such a mammal an effective amount of GM-CSF in conjunction with a vaccine (see abstract). Bonnem indicates that "in conjunction" refers to administration of GM-CSF concurrently, before or following administration of a vaccine (see p. 3, lines 31-32), which would encompass a boost regimen. Bonnem does not teach that the GM-CSF administered is bovine GM-CSF.

Baker teaches a cDNA sequence encoding bovine GM-CSF and methods of expressing bovine GM-CSF in a cell using an expression vector (see Figure 1; column 1, lines 55-68; and column 6, line 13 through column 8, line 25).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to combine the teachings of Taylor, Harris, Bonnem and Baker to create a method of obtaining an immunogenic response comprising administering to a bovine an immunological composition comprising a nucleic acid sequence encoding an the BRSV F gene (an immunogen of the BRSV pathogen) and a cationic lipid (such as DMRIE:DOPE) and also bovine GM-CSF. Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to administer the bovine GM-CSF either together with the DMRIE:DOPE BRSV vaccine composition (in combination) or separately (i.e. sequentially), with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to combine the teachings to create the claimed method in order to create increase the efficacy of the BRSV vaccine by making modifications that were known in the art (as mentioned above, see Harris) such as complexing DMRIE:DOPE to the therapeutic nucleic acid and expressing the BRSV immunogens in order to facilitate the delivery of the plasmids into cells where the immunogen could be expressed (e.g., BRSV F gene, see Taylor) and further comprising bovine GM-CSF to enhance the host's immune response to the BRSV vaccine (see Bonnem and Baker, above). It would have been obvious to add a GM-CSF to the vaccine because Bonnem teaches that GM-CSF enhances the immune response to vaccines (see above). It also would have been obvious to use bovine GM-CSF (taught by Baker) because Taylor teaches that the vaccine is intended for bovines. Furthermore, it would have been obvious to one of skill in the art to administer the vaccine:lipid complex (A) and the bovine GM-CSF (B) in any order (in combination or sequentially) because Bonnem teaches effective administration of the GM-CSF and the vaccine

complex can be concurrently with, or sequentially (either before or following) to administration of the vaccine complex.

Response to Arguments

9. Applicant's arguments filed 6/11/03 have been fully considered but they are not persuasive.

10. Applicants argue each of the references individually, indicating which aspect of each claim is not taught by each reference. For instance, Applicants argue, "None of the cited documents teaches or suggests a method for obtaining an immunogenic response using a DNA vaccine or immunogenic or immunological composition comprising, *inter alia,* a plasmid that expresses DNA encoding an immunogen of a pathogen affecting bovine or porcines in combination with a 'conventional' or recombinant vaccine or immunogenic or immunological composition." (See paragraph bridging p. 9-10 of response filed 6/11/03). Applicants also argue the specific limitations not taught by each reference (see p.11-12).

11. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants also argue that one of ordinary skill in the art would not have been motivated to combine the cited references, and that there would not have been a reasonable expectation of success (See arguments p. 10).

12. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine the references would have been in order to create increase the efficacy of the BRSV vaccine by making modifications that were known in the art (as mentioned above, see Harris) such as complexing DMRIE:DOPE to the therapeutic nucleic acid and expressing the BRSV immunogens in order to facilitate the delivery of the plasmids into cells where the immunogen could be expressed (e.g., BRSV F gene, see Taylor); it is noted that a DNA encoding a polypeptide (in this case an immunogen or pathogen of bovine) must be delivered into a cell in order for the encoded polypeptide to be expressed (and in this case to have the desired immunological response). As indicated, Harris teaches that the cationic amphiphile can facilitate the delivery of a therapeutic nucleic acid into a target cell. Therefore, one of ordinary skill in the art would have been motivated to make the claimed invention for the reasons previously set forth.

13. Regarding the arguments that there would not be a reasonable expectation of success, Applicants argue that it is well known in the art that one problem associated with multivalent compositions is "efficacy interference", or interference with the immunogenic efficacy of an antigen. Applicants indicate the Rabies antigens can interfere with the immunogenic efficacy of other antigens in dogs (See p. 10 of response).

14. In response, it is respectfully pointed out that the cationic amphiphiles have been routinely used, prior to date of the instant invention for, not just for delivering therapeutic nucleic acids into cells in animals, but specifically for delivering polynucleotides encoding immunogenic polypeptides intended to stimulate the immune response of the treated animal. For instance, Jessee et al. (WO 94/27435, cited in IDS Paper #1 as reference AH) teaches that a composition comprising cationic lipids and polynucleotides encoding an antigenic determinant can be used to deliver the polynucleotide of interest to an animal and result in the immunogenic response, such as protective immunity to the antigen, in the treated animal (e.g., see abstract; pages 10-11; p. 14; p.22). Jessee specifically teaches,

> "[T]he lipid/polynucleotide complex can be used as a vaccine to induce active immunity. Preferably, such active immunity is induced in humans, although the invention is not intended to be so limiting. Any animal which may experience the beneficial effects of the vaccines of the invention are within the scope of the animals which may be treated according to the claimed invention." (See p. 22, last paragraph).

Additionally, Jessee indicates that several different cationic lipid formations were tested and all resulted in the desired immune response in the animal (see Example 2, p. 27).

Therefore, it is clear that one of ordinary skill in the art would have been motivated to make the claimed invention and would have had a *reasonable* expectation of success.

Conclusion

15. No claim is allowed.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
Patent Examiner
AU 1635

DAVE T. NGUYEN
PRIMARY EXAMINER